

April 6, 1948.

Dr. Wilson S. Stone,
Dept. Zoology,
University of Texas,
Austin, Texas.

Dear Dr. Stone,

Enclosed are the two manuscripts you have sent. Thank you for the opportunity of seeing them. The work is very impressive, and I hope you will not regard these criticisms as at all derogatory. However, I feel that the concept that the mutation result from the assimilation into the gene of pseudo-metabolites is only one hypothesis among many, although as good a working basis as any of them likewise.

As to the catalase paper, I haven't very much to comment. On p.5, L8 3d Par., I think it would be clearer to write "We may therefore conclude that at such a concentration....# for"Obviously, at such....."

I am not clear what the status of the peroxide in irradiated broth may be. Can 1-5 ppm H_2O_2 be detected with $TiCl_3$ when added to broth? What proportion of peroxide added to broth is recoverable with catalase? Does your catalase react with organic peroxides (according to Sumner and Somers, the specificity of catalase is controversial.)

Perhaps the most dubious paragraph is on p. 7 referring to the mutagenic effects of azide. The point is important enough (from the point of view of "spontaneous mutations") that I think 1) a complete account of the experiment should be given here, and 2) some definite authority given for the assertion that cells inhibited by azide accumulate peroxide. It might be mentioned that azide is not entirely specific for iron enzymes; according to Spiegelman, e.g., it interferes with phosphate transfer in the same way as dinitrophenol. Carbon monoxide or cyanide would be more suitable.

Professor Tatum and I have not had much success with transformations in *E. coli* for which reason I am still anxious to hear of Wyss' results in this direction.

Thank you again for the privilege of seeing these papers in manuscript.

Yours sincerely,

Joshua Lederberg
Assistant Professor of Genetics